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Introduction: An Easy Approach to Cardiovascular Protection

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Heart failure is a significant health problem because of its high morbidity, mortality, and cost of treatment. As the proportion of patients surviving cardiac events such as myocardial infarction increases, the population with heart failure is expected to continue to expand and thus, the associated costs of heart failure will continue to rise.

Heart failure is a progressive disease, characterized by symptoms that can severely debilitate the patient. These symptoms arise as a consequence of inadequate cardiac output and result from multiple and complex systemic responses that are dominated by reflex activation of neurohumoral systems, including the renin-angiotensin-aldosterone and sympathetic nervous systems. Hypertension is a major risk factor for heart failure and plays a key role in the evolution of the disease. As a result of the increased peripheral resistance and enhanced wall tension associated with hypertension, hypertrophy of the left ventricle of the heart may develop, accompanied by fibrosis, which then results in reduced contractility. Ultimately the hypertrophied and fibrosed myocardium is no longer able to maintain normal cardiac output and failure occurs.

Early and aggressive treatment of hypertension reduces the progression of the disease to heart failure and therefore, antihypertensive agents have an important role in slowing the pathogenic adaptations associated with the disease. The central role of angiotensin II in the regulation of blood pressure is the reason why inhibitors of the renin-angiotensin system (RAS) have attracted so much interest both in clinical practice and research; however, the benefits associated with the use of angiotensin converting enzyme (ACE) inhibitors are probably the result of a number of factors, of which blood pressure reduction is only one.

The observation that physicians still limit their use of ACE inhibitors suggests that the benefits of antihypertensive treatment with this drug class are underestimated. There have been several suggestions trying to explain the underusage of ACE inhibitors, the most important of which may be two general misconceptions regarding these agents. One is that they are expensive and the cost associated with ACE inhibitors is not justified based on the outcomes they produce, and the other is that the risk of adverse events associated with their use outweighs their benefits. This is despite significant clinical evidence that demonstrates the beneficial effects of ACE inhibitors on symptomatology, need for hospitalizations and disease progression in heart failure.

Fosinopril is the first of a new class of ACE inhibitors. Fosinopril does not accumulate in patients with renal insufficiency attributable to its dual and compensatory renal and hepatic routes of excretion and this property is of particular interest in patients with severe hypertension and heart failure. In such patients, in whom a concomitant decrease in renal function is often present, compensatory hepatic excretion of fosinopril is useful as dose adjustments are generally not necessary in these patients with impaired ability to excrete drugs through the renal route. In addition, recent data have suggested that the incidence of cough may be lower with fosinopril compared with other members of this pharmacologic class. This might suggest that the ACE inhibitor class is not totally homogenous and that the degree of benefit produced by various members of this class can be differentiated.

The treatment of patients with hypertension has long since moved away from purely controlling blood

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pressure, to considering all risk factors present in a particular patient. Because hypertensive patients often have multiple risk factors for cardiovascular disease it is important to take these into account when initiating therapy and also to consider possible effects of the therapeutic agents chosen on such risk factors. For example, in this context it is interesting that in patients with non–insulin-dependent diabetes, a combination of ACE inhibitor plus thiazide can achieve antihypertensive effects without adversely affecting carbohydrate and lipid metabolism. The additive action of ACE inhibitors and diuretics in the treatment of hypertension has, of course, been demonstrated in numerous studies. Such investigations have demonstrated that the combination is also effective in the elderly and in renally impaired patients.

The effects of pharmacologic reduction of blood pressure on cardiovascular events has also been studied in elderly patients with isolated hypertension. These elderly patients showed a statistically significant reduction in cardiovascular complications. Initial studies with fosinopril have now also shown that there is no increase in withdrawal rate as a result of side effects in these patients. This is particularly important from a clinical viewpoint, as the elderly frequently have a wide range of morbid conditions and accordingly take more medicines. This polytherapy can increase the incidence of drug-related side effects, partly because of potential drug interactions, but also because drug accumulation can occur in association with physiologic deterioration in renal function with age.

Large clinical trials of antihypertensive treatment have not clearly demonstrated gender differences in blood pressure response and outcome; however, the majority of patients in these trials were men. As with men, hypertensive women also exhibit an increased risk for both coronary disease and stroke compared to normotensive controls; however, the incidence is lower in women under 65 years of age. For this reason, there have been discussions relating to whether or not treatment thresholds should differ between men and women. Notwithstanding, it is important that hypertension in women be treated as vigorously as in men to avoid major complications, which have been found to be associated with a prognosis possibly even worse than in men.

As a result of the increasing cost of health care and the limited resources available, it has become more difficult to allocate resources efficiently and effectively in the health care system. This environment has led to the development of pharmacoeconomic studies, which have been designed in response to the need for assessment of the economic benefits of a product before its acceptance in the market. Conventionally, ACE inhibitors have been considered expensive agents compared to more longer established agents. Cost effectiveness analyses of ACE inhibitors for the treatment of heart failure are, however, beginning to show these agents to be cost-effective by markedly reducing the cost of hospitalization, diagnostic procedures, and of the general management of these patients. All in all, it cannot be emphasized enough that there are probably few alternative ways of spending health care money that, in the long term, provide a better return on investment in terms of quality of life, to providing elderly patients with hypertension and congestive heart failure optimal therapy with ACE inhibitors.